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CLAIMS

What is claimed is:

1. A method for identifying a compound that modulates the activity of a PAP phosphatase enzyme, comprising:
   (a) contacting a compound with a PAP phosphatase polypeptide; and
   (b) detecting modulation of the activity of said PAP phosphatase polypeptide.
2. The method of claim 1, comprising selecting said compound as a PAP phosphatase modulating compound if said compound modulates the activity of said PAP phosphatase polypeptide.
3. The method of claim 1, wherein said PAP phosphatase polypeptide is a BPntase polypeptide.
4. The method of claim 2, wherein contacting said compound with said PAP phosphatase polypeptide comprises growing at least one recombinant yeast strain expressing said PAP phosphatase polypeptide in a minimal media lacking methionine and containing said compound, such that said compound contacts said recombinant yeast.
5. The method of claim 4, wherein said recombinant yeast strain is selected from the group consisting of *hal2*::Hal2p, *hal2*::BPntase, and combinations thereof.
6. The method of claim 5, wherein said *hal2*::BPntase strain is a *hal2*::hBPntase.
7. The method of claim 4, wherein detecting modulation of the activity of said PAP phosphatase polypeptide comprises measuring for growth of said recombinant yeast strain.
8. The method of claim 7, wherein measuring for growth of said recombinant yeast strain comprises measuring a change in optical density.
9. The method of claim 7, wherein selecting said compound as a PAP phosphatase modulating compound comprises selecting said compound

as said PAP phosphatase modulating compound if growth of said recombinant yeast strain is inhibited.

10. The method of claim 9, wherein said yeast strain is a combination of said *hal2*::Hal2p strain and said *hal2*::BPntase strain grown concurrently in minimal media lacking methionine and containing said compound and said compound is selected as said PAP phosphatase modulating compound if at least growth of said *hal2*::BPntase yeast strain is inhibited.

11. The method of claim 1, wherein detecting modulation of the activity of said PAP phosphatase polypeptide comprises detecting binding of said compound to said PAP phosphatase polypeptide.

12. The method of claim 11, wherein said PAP phosphatase polypeptide is a mammalian BPntase polypeptide.

13. The method of claim 12, wherein said compound binds at an active site of said BPntase enzyme.

14. The method of claim 13, wherein said active site is a lithium binding site.

15. The method of claim 13, wherein said active site is a low affinity Mg^{2+} binding site.

16. The method of claim 1, wherein detecting modulation of the activity of said PAP phosphatase polypeptide comprises detecting inhibition of the activity of said PAP phosphatase polypeptide.

17. The method of claim 16, wherein said PAP phosphatase polypeptide is a mammalian BPntase polypeptide.

18. A method for identifying a compound that modulates the activity of a sulfur assimilation pathway enzyme, comprising:

(a) contacting a compound with a sulfur assimilation pathway enzyme; and

(b) detecting modulation of the activity of said sulfur assimilation pathway enzyme.

19. The method of claim 18, wherein said sulfur assimilation pathway enzyme is selected from the group consisting of ATP sulfurylase, APS

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kinase, sulfotransferase, PAPS reductase, PAP phosphatase and combinations thereof.

20. The method of claim 19, wherein said sulfur assimilation pathway enzyme is a yeast sulfur assimilation pathway enzyme.

21. The method of claim 20, wherein said ATP sulfurylase enzyme is a Met3 enzyme and said APS kinase enzyme is a Met14 enzyme.

22. The method of claim 19, wherein said sulfur assimilation pathway enzyme is a mammalian sulfur assimilation pathway enzyme.

23. The method of claim 22, wherein said ATP sulfurylase enzyme and said APS kinase enzyme together are a bifunctional PAPS synthetase enzyme.

24. The method of claim 18, wherein detecting modulation of the activity of said sulfur assimilation pathway enzyme comprises detecting binding of said compound to said sulfur assimilation pathway enzyme.

25. The method of claim 18, wherein detecting modulation of the activity of said sulfur assimilation pathway enzyme comprises detecting inhibition of the activity of said sulfur assimilation pathway enzyme.

26. The method of claim 18, wherein detecting modulation of the activity of said sulfur assimilation pathway enzyme comprises detecting a change in the amount of a sulfur assimilation pathway enzyme product.

27. The method of claim 26, wherein said sulfur assimilation pathway product is selected from the group consisting of APS, PAPS, PAP, AMP, cAMP, and combinations thereof.

Product & Substrate are the same?

28. The method of claim 18, wherein detecting modulation of the activity of said sulfur assimilation pathway enzyme comprises detecting a change in the amount of a sulfur assimilation pathway enzyme substrate.

29. The method of claim 28, wherein said sulfur assimilation pathway enzyme substrate is selected from the group consisting of ATP, APS, PAPS, PAP, AMP, and combinations thereof.

30. A transgenic non-human vertebrate animal having incorporated into its genome a modified gene encoding a BPntase polypeptide.

31. The transgenic animal of claim 30, wherein said modified gene encodes a biologically active human BPntase polypeptide.

32. The transgenic animal of claim 31, wherein said modified gene is incorporated into said genome so as to confer overexpression in said animal of said biologically active human BPntase polypeptide.

33. The transgenic animal of claim 30, wherein said modified gene is disrupted wherein said disrupted modified gene results in one of expression of a nonfunctional BPntase polypeptide and substantially no expression of a BPntase polypeptide.

34. The transgenic animal of claim 30, wherein expression of said BPntase polypeptide is conferred in a tissue or blood of said transgenic animal.

35. The transgenic animal of claim 34, wherein said tissue is selected from the group consisting of kidney tissue, brain tissue, liver tissue, intestinal tissue, skin tissue, heart tissue, lung tissue, spleen tissue, bone marrow, and combinations thereof.

36. The method of claim 33, wherein said disruption of said gene is a homozygous disruption.

37. A transgene construct comprising an isolated BPntase gene encoding a BPntase polypeptide cloned into a vector.

38. The transgene construct of claim 37, wherein said vector is a plasmid.

39. An isolated cell comprising said transgene construct of claim 38.

40. A method of identifying a compound for treating a toxic effect resulting from a therapeutic treatment, comprising:

(a) obtaining a transgenic non-human vertebrate animal having incorporated into its genome a disruption of a gene encoding a BPntase polypeptide, wherein said disruption results in said transgenic animal exhibiting said toxic effect;

(b) administering said compound to said transgenic animal; and

(c) observing said transgenic animal for a change in said transgenic animal indicative of amelioration of said effect.

41. The method of claim 40, wherein said therapeutic treatment is a lithium treatment for a neurological disorder.

42. The method of claim 41, wherein said neurological disorder is bipolar disorder.

43. The method of claim 40, wherein said disruption of said gene is a homozygous disruption.

44. The method of claim 40, wherein disruption of a gene encoding a BPntase polypeptide is conferred to a tissue or blood of said transgenic animal.

45. The method of claim 44, wherein said tissue is selected from the group consisting of kidney tissue, brain tissue, liver tissue, intestinal tissue, skin tissue, heart tissue, lung tissue, spleen tissue, bone marrow, and combinations thereof.

46. The method of claim 40, wherein said transgenic animal is a mouse.

47. The method of claim 40, wherein said toxic effect is selected from the group consisting of emesis, diarrhea, organ dysfunction, hypothyroidism, and combinations thereof.

48. The method of claim 47, wherein said organ dysfunction is kidney dysfunction.

49. A method for treating lithium-related toxicity, comprising administering to a subject suffering from said toxicity a therapeutically effective amount of a compound that modulates the activity of at least one sulfur assimilation pathway enzyme.

50. The method of claim 49, wherein said method comprises treating a lithium-related toxic effect selected from the group consisting of nausea, emesis, diarrhea, organ dysfunction, hypothyroidism, and combinations thereof.

51. The method of claim 50, wherein said organ dysfunction is kidney dysfunction.

52. The method of claim 49, wherein said sulfur assimilation pathway enzyme is selected from the group consisting of ATP sulfurylase, APS kinase, sulfotransferase, PAPS reductase and combinations thereof.

53. The method of claim 49, wherein said sulfur assimilation pathway enzyme is a mammalian sulfur assimilation pathway enzyme.

54. The method of claim 53, wherein said ATP sulfurylase enzyme and said APS kinase enzyme together are a bifunctional PAPS synthetase enzyme.

55. The method of claim 49, wherein said compound is chlorate.

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56. A method of identifying a compound that modulates the activity of a BPntase polypeptide, comprising modeling an interaction between said compound and a target moiety on said BPntase polypeptide.

57. The method of claim 56, wherein modeling is computer modeling.

58. The method of claim 56, wherein said interaction is binding of said compound to said BPntase polypeptide by hydrogen bonding, van der Waal's binding, or both hydrogen bonding and van der Waal's bonding.

59. The method of claim 56, wherein said target moiety is a druggable region.

60. The method of claim 59, wherein said druggable region is a lithium binding site.

61. The method of claim 60, wherein said target moiety is a low affinity Mg^{2+} binding site.

62. The method of claim 61, wherein said target moiety is a cluster of amino acid residues fixed at specific spatial points as determined by secondary structure of said BPntase peptide, said residues being Asp-51, Glu-74, Asp-117, and Leu-119.